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EXAMINER	
CHEN, SHIN LIN	
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1632	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/722,661	BERNS ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89-95,99 and 101-127* is/are pending in the application.

4a) Of the above claim(s) *99* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *89-95 and 101-127* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5-19-08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment and the declaration by Dr. Anton Berns filed 5-19-08 have been entered. Claims 89, 90, 93-95, 105, 108, 112-115 and 121-126 have been amended. Claims 96-98 and 100 have been canceled. Claims 89-95, 99 and 101-127 are pending. Claims 89-95 and 101-127 are under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 89-95 and 101-127 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants' amendment filed 5-19-08 necessitates this new ground of rejection.

The phrase "flanking sequences that are obtained from said inbred strain of animal" in lines 11-12 of claim 89 is vague and renders the claim indefinite. It is unclear what "said inbred strain of animal" refers to. It is unclear whether the phrase "said inbred strain of animal" refers to "an inbred strain of mice" in line 2, "an inbred strain of mice" in line 3, or "an inbred strain of mice" in line 7. Claims 90-95 and 101-127 depend from claim 89 but fail to clarify the indefiniteness.

Applicants argue that the claims have been amended to read on "an inbred strain of mice", which has a consistent meaning throughout claim 89 (amendment, p. 7-8). This is not found persuasive because the phrase "said inbred strain of animal" is still in line 12 of claim 89

and applicants still fail to address the issue that whether the phrase "said inbred strain of animal" refers to "**an** inbred strain of mice" in line 2, "**an** inbred strain of mice" in line 3, or "**an** inbred strain of mice" in line 7 as discussed above.

The phrase "said inbred strain of mice" in claims 115 and 121-124 is vague and renders the claim indefinite. It is unclear what "said inbred strain of mice" refers to. It is unclear whether the phrase "said inbred strain of mice" refers to "an inbred strain of mice" in line 2, "an inbred strain of mice" in line 3, or "an inbred strain of mice" in line 7.

3. Claim 89 recites the limitation "said inbred strain of animal" in line 12. There is insufficient antecedent basis for this limitation in the claim.

4. Claim 105 recites the limitation "the same individual animal" in lines 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 89-95 and 101-127 remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Capecchi et al. (IDS, C06-1989) and is repeated for the reasons set forth in the preceding Official action mailed 2-5-08. Applicant's arguments filed 5-19-08 have been fully considered but they are not persuasive.

Applicants cite Thomas and Capecchi, 1987 (Thomas) and argue that Capecchi use the term "homology" to mean the length of the homologous regions rather than to the degree of sequence identity. Capecchi discusses the effect of the "extent of homology" by using the unit "kilobases" and "base pair" of homology. Thomas describes using targeting vectors containing different lengths of Hprt DNA to test frequency of homologous recombination. The targeting DNA and target DNA are from different mouse trains, and 2-fold increase in homology increased the gene-targeting frequency by 20-fold. Therefore, Thomas and Capecchi refer to the length of endogenous and targeting Hprt sequences and not to the degree of nucleotide sequence similarity (amendment, p. 9-12). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 2-5-08. The term "homology" implies similarity between sequences and encompasses 100% identity. Thomas discloses that the parameters that influence

success of gene-targeting include "extensive homology between the homing **sequence** and the target **sequence**" (e.g. Thomas, p. 510, left column). One of ordinary skill in the art reading "Thomas" would understand that the phrase "extensive homology between the homing sequence and the target sequence" mean the higher the similarity of nucleotide sequence between the homing sequence and the target sequence the better success of gene-targeting would be. Although Thomas might refer to the sequence length regarding "2-fold increase in homology increased the gene-targeting frequency by 20-fold", however, it should be noted that Thomas use the same gene, Hprt gene, for gene targeting experiment. Although they are from different mouse strains but it is expected that their sequences would be very similar to each other. When the sequence length increases, the number of identical nucleotide would also increase between the targeting sequence and the target sequence. When one of ordinary skill in the art performs "homologous recombination", one would use the **same** gene rather than totally different genes, which would have very different nucleotide sequences. One of ordinary skill in the art would not use a very long DNA sequence, which has very different nucleotide sequence as compared to the target sequence (low homology), in a targeting vector to perform a "**homologous** recombination" at the target sequence. Therefore, the phrase "extent of homology" discussed by Thomas could refer to the length of the sequence and also the number of similar or identical nucleotides between the targeting sequence and the target sequence. The phrase "extent of homology" does not exclude the requirement of sequence identity between the targeting sequence and the target sequence, and the phrases "5 kilobases of homology" and "25-50 base pairs of homology" discussed by Capecchi would imply similarity between nucleotide sequences.

Applicants argue that Capecchi fails to teach using DNA from the same mouse strain in the targeting DNA and the target DNA and the phrase "extensive homology" recited by Thomas refers to the length of homologous DNA in the targeting vector. Applicants further argue that no one at the time of the invention practice homologous recombination by using DNA from the same mouse strain in targeting DNA and target DNA. One of ordinary skill in the art would not find a reasonable expectation of success in achieving the recombination frequency of the claimed invention. Applicants cite declaration by Dr. Anton Berns dated March 14, 1995 (submitted 8-2-07 and resubmitted 5-19-08) and argue that scientist in the field of gene targeting at the time of the invention were using targeting DNA from a mouse strain that is different from the targeted cells, and the increase of the length of the homologous region would increase the efficiency of gene targeting. The increase in efficiency was not believed to be related to the degree of sequence identity between the flanking sequence of the targeting DNA and the target cells (amendment, p. 13-14).). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 2-5-08 and the reasons set forth above. The phrase "extent of homology" discussed by Thomas could refer to the length of the sequence and also the number of similar or identical nucleotides between the targeting sequence and the target sequence. The phrase "extent of homology" does not exclude the requirement of sequence identity between the targeting sequence and the target sequence, and the phrases "5 kilobases of homology" and "25-50 base pairs of homology" discussed by Capecchi would imply similarity between nucleotide sequences. It would be obvious for one of ordinary skill in the art to use identical nucleotide sequence or high sequence identity nucleotide sequence in targeting DNA and target DNA for "homologous recombination" in order to achieve higher homologous recombination frequency.

It would be obvious for one of ordinary skill in the art to use targeting DNA sequence obtained form the mouse strain as the target cells, and homologous recombination frequency using the DNA from same mouse strain would be inherent to the mouse strain used. As discussed above under 35 U.S.C. 112 second paragraph, it is unclear whether the phrase "said inbred strain of mice" refers to "an inbred strain of mice" in line 2, "an inbred strain of mice" in line 3, or "an inbred strain of mice" in line 7. It is noted that claims 89-95, 101-104, 106-124, 126 and 127 read on using targeting DNA sequence and target DNA sequence obtained from different mouse strains and it would also be obvious to one of ordinary skill for the reasons set forth above.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 89-95, 101-120 and 122-127 remain rejected under 35 U.S.C. 102(e) as being anticipated by Capecchi et al. (US Patent No. 5,464,764) and is repeated for the reasons set forth in the preceding Official action mailed 2-5-08. Applicant's arguments filed 5-19-08 have been fully considered but they are not persuasive.

Applicants argue that the term "homology", by reference Capecchi and reference Thomas, means "a common evolutionary origin" and not the meaning of "sequence identity".

The term "homology" used in '764 patent conveys the evolutionary relationship between targeting DNA and target DNA and 100% homology means they are from same animal species. The x-axis of Figure 4 of '764 is labeled "HOMOLOGY (kb)" from 0 to 14 kb. It is the number of kilobases of Hprt sequence not a measure of nucleotide sequence identity. Applicants cite reference Capecchi (1989) and Thomas (1987) and reiterates that the term "extent of homology" refers to the length of endogenous and targeting hprt sequence which are of mouse origin. Applicants reiterate that the target DNA and targeting DNA in reference Thomas are from different mouse strains. The term "100% sequence homology" in '764 refers to the relationship between the Hprt sequences in the PNS vector and in the ES cells (amendment, p. 14-16). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 2-5-08 and the reasons set forth above. The term "homology" implies similarity between sequences and encompasses 100% identity. The phrase "extent of homology" discussed by Thomas could refer to the length of the sequence and also the number of similar or identical nucleotides between the targeting sequence and the target sequence. The phrase "extent of homology" does not exclude the requirement of sequence identity between the targeting sequence and the target sequence. When one of ordinary skill in the art performs "homologous recombination", one would use the **same** gene rather than totally different genes, which would have very different nucleotide sequences. One of ordinary skill in the art would not use a very long DNA sequence, which has very different nucleotide sequence as compared to the target sequence (low homology), in a targeting vector to perform a "**homologous** recombination" at the target sequence.

Capecchi ('764) teaches "Substantial homology is necessary between these portions in the PNS vector and the target DNA to insure targeting of the PNS vector to the appropriate region of the genome" and Figure 4 compare absolute frequency of homologous recombination and the amount of **100% sequence homology** in the first and second DNA sequences of the PNS vectors (e.g. column 6, lines 55-58, Figure 4). Capecchi ('764) further teaches that "[t]he degree of homology between the vector and target sequences influence the frequency of homologous recombination between the two sequences. One hundred percent sequence homology is most preferred" (e.g. column 20, lines 33-37). "Although as few as 25 bp of 100% homology are required for homologous recombination in mammalian cells… longer regions are preferred, e.g. 500 bp, more preferably, 5000 bp, and most preferably, 25000 bp for each homologous portion" and "[p]referably, the homologous portions of the PNS vector will be 100% homologous to the target DNA sequence, as increasing the amount of non-homology will result in a corresponding decrease in the frequency of gene targeting" (e.g. column 20, lines 43-53). It appears that not only the nucleotide sequence homology (100% sequence homology) between the targeting DNA and the target DNA is important but also the length of the 100% homologous DNA sequence is important to the recombination frequency. One of ordinary skill in the art would understand the phrase "100% sequence homology" means 100% nucleotide sequence homology. The length of 0 to 14 kb means the length of nucleotide sequence that is homologous to each other. Therefore, Capecchi ('764) teach using targeting DNA that has the same nucleotide sequence as that of target DNA in target cells. It would be obvious to one of ordinary skill in the art to use longer homologous DNA sequence in targeting DNA because longer homologous or identical sequence

between targeting DNA and target DNA would provide better frequency of homologous recombination as evidenced by Capecchi ('764).

Applicants argue that '764 patent uses the term "100% sequence homology" to describe an evolutionary relationship, i.e. target DNA and targeting DNA are DNA sequences of the same gene from the same species of animal (e.g. mouse) (amendment, p. 16). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 2-5-08 and the reasons set forth above. If the term "100% sequence homology" is used to describe an evolutionary relationship, i.e. target DNA and targeting DNA are DNA sequences of the same gene from the same species of animal (e.g. mouse), then it would be obvious to one of ordinary skill to use targeting DNA and target DNA of the same gene from the same strain of mouse because the same gene from the same mouse strain would be more likely to be "100% sequence homology" in terms of evolutionary relationship.

Applicants argue that Figure 3 shows one difference between the nucleotide sequence of the first DNA in the PNS vector and the target DNA. Applicants argue that the phrase "substantial homology is necessary between portions in the PNS vector and the target DNA..." recited by Examiner discuss the accuracy of the targeting to an appropriate region of the genome and not the higher frequency of homologous recombination with a target gene. Applicants further argue that the phrase "the word 'homology' is used here to describe participants in homologous recombination, which are generally identical" recited by Capecchi (1989) would render one of ordinary skill in the art to understand that the flanking sequence in vector and target DNA in Thomas are homologous and not 100% base-by-base identical, and the 14 kb genomic sequence used by Thomas had not been sequenced and compared, and shown to be

100% identical (amendment, p. 16-17). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 2-5-08 and the reasons set forth above. One nucleotide difference between the PNS vector and the target DNA sequence demonstrates that the first and second DNA sequences in the PNS vector are almost 100% identical to the corresponding sequences in the target DNA. The phrase recited by Capecchi (1989) clearly means that the term "homology" means "identical", therefore, the phrase "100% sequence homology" would imply "100 sequence identity". Further, there is no evidence of record that shows the 14 kb genomic sequence has not been sequence and compared to be 100% identical.

Applicants argue that five fold increase in "sequence homology" is the increase from 2.9 kb to 14.3 kb and the term "sequence homology" does not mean "sequence identity" (amendment, p. 17-18). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 2-5-08 and the reasons set forth above.

Applicants argue that the "neo" gene is referred to as "nonhomology" in Capecchi (1989) and it possess a different evolutionary origin from the mouse target DNA. Therefore, Capecchi use the term "homology" to indicate a common evolutionary origin as endorsed by Reeck (amendment, p. 18). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 2-5-08 and the reasons set forth above. The "neo" gene is considered "nonhomology" because the neo gene is an exogenous gene that has very different nucleotide sequence from its flanking sequence at the target DNA. The flanking sequence of the target DNA is identical or has high sequence homology to the corresponding sequence of the targeting vector, therefore, the recombination between these two sequences is "homologous recombination".

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 89, 90 and 121 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Capecchi et al. (US Patent No. 5,464,764) in view of Koller et al. (US Patent No. 5,416,260) and is repeated for the reasons set forth in the preceding Official action mailed 2-5-08. Applicant's arguments filed 5-19-08 have been fully considered but they are not persuasive.

Applicants argue that the teachings of the prior art cited by Examiner extend only as far as using DNA from the same animal species and there is no hint or suggestion in the references that an improvement might by achieved through the use of target DNA and targeting DNA from the same inbred strain. The frequency obtained by practicing the instant invention was unpredictable at the time of the invention. Without the present invention, one of ordinary skill in

the art would continue to use targeting DNA and target DNA from different strains of mouse, and try to increase recombination frequency by maximizing the extent of the overlapping homologous sequences. Applicants further argue that the targeting DNA and its corresponding homologous DNA sequence in target DNA are obtained from different mouse strains in either '764 or '260 (amendment, p. 18-20). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 2-5-08 and the reasons set forth above. Capecchi ('764) teaches that "[t]he degree of homology between the vector and target sequences influence the frequency of homologous recombination between the two sequences. One hundred percent sequence homology is most preferred" (e.g. column 20, lines 33-37). "Although as few as 25 bp of 100% homology are required for homologous recombination in mammalian cells… longer regions are preferred, e.g. 500 bp, more preferably, 5000 bp, and most preferably, 25000 bp for each homologous portion" and "[p]referably, the homologous portions of the PNS vector will be 100% homologous to the target DNA sequence, as increasing the amount of non-homology will result in a corresponding decrease in the frequency of gene targeting" (e.g. column 20, lines 43-53). It appears that not only the nucleotide sequence homology (100% sequence homology) between the targeting DNA and the target DNA is important but also the length of the 100% homologous DNA sequence is important to the recombination frequency. Capecchi ('764) clearly demonstrates that the sequence identity and the length of homologous sequence are important factor in determining the recombination frequency. It would be prima facie obvious for one of ordinary skill in the art to use targeting DNA sequence that is 100% homologous (100% identical) to the corresponding sequence at target DNA in order to obtain higher recombination frequency in view of the teachings of Capecchi ('764). Thus, it would be obvious

for one of ordinary skill in the art to use targeting DNA and target DNA that are obtained from the same mouse strain, which would have 100% identical sequence. Further, as discussed above, if the term "100% sequence homology" is used to describe an evolutionary relationship, i.e. target DNA and targeting DNA are DNA sequences of the same gene from the same species of animal (e.g. mouse), then it would be obvious to one of ordinary skill to use targeting DNA and target DNA of the same gene from the same strain of mouse because the same gene from the same mouse strain would be more likely to be "100% sequence homology" in terms of evolutionary relationship.

14. Claims 89-95 and 101-127 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Capecchi et al. (IDS, C06-1989) or Capecchi et al. (US Patent No. 5,464,764) each in view of Doetschman et al., 1987 (Nature, Vol. 330, p. 576-578, IDS-C14) and is repeated for the reasons set forth in the preceding Official action mailed 2-5-08. Applicant's arguments filed 5-19-08 have been fully considered but they are not persuasive.

Applicants argue that there is nothing in Doetschman that suggests "2.5 and 5 kb of DNA in common with the target locus" means 100% identical to the corresponding sequences in the target locus, and the targeting vector and target DNA sequence are obtained from different mouse strains. The term "common" as used in Doetschman means targeting and target DNA with a common evolutionary origin, i.e. from the same species of animal. Applicants further argue that Capecchi C06 and '764 patent does not teach using flanking sequences in the targeting DNA that are 100% identical to the corresponding sequences in the genome of the target cells (amendment, p. 20-22). This is not found persuasive because of the reasons set forth in the

preceding Official action mailed 2-5-08 and the reasons set forth above. Even if Doetschman does not necessarily mean 100% identical flanking sequence in targeting vector to corresponding sequence in the target DNA sequence, Capecchi ('764) clearly demonstrates that the sequence identity and the length of homologous sequence are important factor in determining the recombination frequency. It would be prima facie obvious for one of ordinary skill in the art to use targeting DNA sequence that is 100% homologous (100% identical) to the corresponding sequence at target DNA or use longer 100% homologous sequence in order to obtain higher recombination frequency in view of the teachings of Capecchi ('764). Thus, it would be obvious for one of ordinary skill in the art to use targeting DNA and target DNA that are obtained from the same mouse strain, which would have 100% identical sequence. Further, as discussed above, if the term "100% sequence homology" is used to describe an evolutionary relationship, i.e. target DNA and targeting DNA are DNA sequences of the same gene from the same species of animal (e.g. mouse), then it would be obvious to one of ordinary skill to use targeting DNA and target DNA of the same gene from the same strain of mouse because the same gene from the same mouse strain would be more likely to be "100% sequence homology" in terms of evolutionary relationship.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 89-95 and 101-127 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,653,113. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the claims.

17. Claims 89-95 and 101-127 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 5,789,215. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the claims.

Applicants' indication of submitting a Terminal Disclaimer under 37 C.F.R. 1.321(c) upon indication of allowable subject matter is acknowledged.

Conclusion

No claim is allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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